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This listing of claims will replace all prior versions, and listings, of claims in the application.

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Listing of Claims:

Claims 1-7. (Canceled)

- 8. (Previously Presented) The compound of claim 112 wherein said amino acid is amino caproic acid.
- 9. (Previously Presented) The compound of claim 112 wherein said $X_{4'}$ is the side chain of glutamic acid.
- 10. (Previously Presented) The compound of claim 112 wherein said X_6 has one of the formulas:

wherein:

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SS is a solid support; X_7 is O or CH₂; Bx is a nucleobase, C_4 - C_{14} heterocyclyl or hydrogen; z is an integer from 1 to 50; and u is an integer from 2 to 5.

11. (Previously Presented) The compound of claim 112 wherein said R_1 is dimethoxytrityl.

Claims 12-31 (Canceled).

- 32. (Previously Presented) The method of claim 104 wherein W₁ has the formula -O-(CH₂)_n-NH-, wherein n is from 1 to about 10.
- 33. (Original) The method of claim 32 wherein n is 6.
- 34. (Canceled)
- 35. (Previously Presented) The method of claim 104 wherein R_1 is dimethoxytrityl, A has the formula -O-(CH₂)_n-NH- where n is 6, m is 2, R_4 is t-butoxy, R_5 is trifluoroacetoyl, R_6 is -C(=O)-CH(CH₃)₂, and R_{30} is FMOX.

Claims 36-39 (Canceled).

- 40. (Previously Presented) The method of claim 105 wherein R_1 is dimethoxytrityl, W_1 has the formula -O-(CH₂)_n-NH- where n is 6, m is 2, R_4 is t-butoxy, R_5 is trifluoroacetoyl, R_6 is -C(=O)-CH(CH₃)₂, and R_{30} is FMOX.
 - 41. (Canceled)
- 42. (Previously Presented) The method of claim 26 wherein said compound IX is prepared by reacting folic acid:

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$$\begin{array}{c|c} O & & & & & \\ \hline \\ HO & O & & & \\ \hline \\ HO & O & & \\ \hline \\ \end{array}$$

with a reagent effective to form pterin aldehyde:

and

protecting the amino group of said pterin aldehyde.

Claims 43-62 (Canceled).

- 63 (Previously Presented). The compound of claim [[107]] 115 wherein m is 2.
- 64. (Original) The compound of claim 63 wherein W_1 is $-O-(CH_2)_6$ -NH-.
 - 65. (Previously Presented) The compound of claim 64 wherein R_4 is t-butoxy.

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66 (Original). The compound of claim 65 wherein R_1 is dimethoxytrityl, R_5 is trifluoroacetoyl, and R_6 is -C(=O)-CH(CH₃)₂.

67 (Original). The compound of claim 66 wherein q is 0.

Claims 68-71 (Canceled).

72 (Original). A composition comprising a compound of claim 63, said composition being substantially free of a compound of formula XVA, XVB, XVC or XVD:

$$R_1$$
-O B
 R_{21}
 q
 R_{20}
 W_{15}
 $X V A$

$$\begin{bmatrix} & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & &$$

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W 15
$$\begin{bmatrix} O & B \\ R_{21} \end{bmatrix}$$
 $\begin{bmatrix} Q & B \\ R_{20} & R_{21} \end{bmatrix}$

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wherein W_{15} has the formula:

Claims 73-78 (Canceled).

79 (Previously Presented). The compound of claim 116 wherein m is 2.

80 (Original). The compound of claim 79 wherein W_1 is -O-(CH_2)_n-NH-wherein n is from 1 to about 10.

81 (Original). The compound of claim 80 wherein n is 6.

Claims 82-87 (Canceled).

- 88. (Previously Presented) The compound of claim 117 wherein m is 2.
- 89. (Original) The compound of claim 88 wherein W_1 is -O-(CH_2)_n-NH- wherein n is from 1 to about 10.
 - 90. (Original) The compound of claim 89 wherein n is 6.

Claims 91 and 92 (Canceled).

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93 (Previously Presented). The compound of claim 112 wherein said R_4 is a hydroxyl group protected with C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl or C_2 - C_{20} alkynyl.

Claims 94-103 (Canceled).

104 (Previously Presented) A synthetic method comprising the steps of:

(a) providing a compound of formula IA, IB, IC or ID:

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$$R_1$$
-O B
 R_{21}
 Q
 W_{1a}
 R_{21}
 R_{21}
 R_{21}
 R_{21}
 R_{21}

$$W_1a$$
 Q
 R_{21}
 Q
 R_{21}
 Q
 R_{20}
 R_{21}

IC

IA

$$R_1$$
—O B
 W_1a
 q
 R_{20} R_{21}
ID

wherein:

 W_{1a} is $W_{1b}\mbox{-H},$ OH, NH_2 or SH, where W_{1b} is a linking group;

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 R_1 is H or a hydroxyl protecting group;

B is a nucleobase;

each R₂₁ is H, OH, F, or a group of formula Z-R₂₂-(R₂₃)_v;

Z is O, S, NH, or N- R_{22} - $(R_{23})_{\nu}$

 R_{22} is C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, or C_2 - C_{20} alkynyl;

R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

v is from 0 to about 10;

or R_{21} has one of the formulas:

$$(CH_2)_{y_2}$$
 O E

$$--(O)_{y_1} - (CH_2)_{y_2} - O - N - (CH_2)_{y_2} - O - E$$

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wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1 - C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

q is from zero to about 50, provided that when said compound has formula ID, q is at least 1;

M is an optionally protected internucleoside linkage;

(b) reacting said compound of formula I with a compound of formula II:

 Π

wherein:

R₃₀ is an amino protecting group;

 X_3 is a group of formula XII:

XII

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wherein m is 1 or 2;

 R_4 is a hydroxyl group, or a protected hydroxyl group; to form a compound of formula IVA, IVB, IVC, or IVD:

$$R_1$$
— O
 M
 W_4
 Q
 R_{20}
 R_{21}
 IVD

wherein:

W₄ has the formula:

IVC

$$\begin{cases} - W_1 - C - X_3 - N - R_{30} \\ - W_1 - C - X_3 - N - R_{30} \end{cases}$$

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where W₁ is a linking group, O, NH, or S; and

treating said compound of formula IVA, IVB, IVC or IVD with a deprotecting reagent to form a compound of formula VA, VB, VC or VD:

$$R_{1} = 0$$

$$R_{21}$$

$$R_{21}$$

$$R_{20}$$

$$R_{21}$$

$$R_{21}$$

$$R_{20}$$

$$R_{21}$$

$$R_{21}$$

$$R_{21}$$

$$R_{21}$$

$$R_{21}$$

$$R_{21}$$

$$R_{20}$$

$$R_{21}$$

$$R_{20}$$

$$R_{21}$$

$$R_{20}$$

$$R_{21}$$

wherein W₅ has the formula:

$$\left\{ \begin{matrix} \mathrm{O} \\ -\mathrm{W}_{1}-\mathrm{C}-\mathrm{X}_{3}-\mathrm{NH}_{2} \end{matrix}
ight\}$$
 and

V D

VC

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(c) condensing said compound of Formula V with a compound of Formula VI:

$$O \longrightarrow N \longrightarrow NH$$

$$R_5 \longrightarrow N \longrightarrow NH$$

$$R_6$$

VI

wherein:

R₅ is H or an amino protecting group;

R₆ is H or an amino protecting group;

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to form a compound of Formula VIIA, VIIB, VIIC, or VIID:

$$R_1$$
-O B
 R_{21}
 Q
 R_{20}
 R_{20}

$$\begin{array}{c|c} R_1\text{-}O & B \\ \hline \\ M & R_{21} \\ \hline \\ W_7 & R_{21} \end{array}$$

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$$\begin{array}{c|c} W_{7} & & & \\ & & & \\ M & & & \\ & & & \\ R_{20} & & \\ R_{21} & & \\ \end{array}$$

$$R_1$$
— O B W_7 q O B R_{20} R_{21}

VIID

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wherein W₇ has the Formula:

$$\{-W_1-C-X_3-NH \}$$

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105. (Previously Presented) A synthetic method comprising the steps of:

(a) providing a compound of formula IA, IB, IC or ID:

ΙB

$$R_1$$
—O O B W_1a q O B R_{20} R_{21}

ID

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wherein:

W_{1a} is W_{1b}-H, OH, NH₂ or SH, where W_{1b} is a linking group;

 R_1 is H or a hydroxyl protecting group;

B is a nucleobase;

each R₂₁ is H, OH, F, or a group of formula Z-R₂₂-(R₂₃)_v;

Z is O, S, NH, or N-
$$R_{22}$$
- $(R_{23})_v$

 R_{22} is C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, or C_2 - C_{20} alkynyl;

R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

v is from 0 to about 10;

or R_{21} has one of the formulas:

$$- (O)_{y_1} - (CH_2)_{y_2} - O - N - (CH_2)_{y_2} - O - E$$

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wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1 - C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

q is from zero to about 50, provided that when said compound has formula ID, q is at least 1;

M is an optionally protected internucleoside linkage;

(b) reacting said compound of formula I with a compound of formula II:

$$R_{30}$$
—NH— X_3 -C—OH

 \mathbf{II}

wherein:

R₃₀ is an amino protecting group;

 X_3 is a group of formula XII:

XII

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wherein m is 1 or 2;

 R_4 is a hydroxyl group, or a protected hydroxyl group; to form a compound of formula IVA, IVB, IVC, or IVD:

$$R_1$$
-O B
 R_{21}
 Q
 R_{20}
 W_4
IV A

$$W_{4} = \begin{bmatrix} O & B \\ R_{21} & q \\ O & B \\ R_{20} & R_{21} \end{bmatrix}$$

IVC

$$R_1$$
— O
 M
 W_4
 Q
 R_{20}
 R_{21}
IV D

wherein:

W₄ has the formula:

$$\left\{ -W_{1}-\overset{O}{\overset{\parallel}{C}}-X_{3}-\overset{N}{\overset{}{H}}-R_{30}\right\}$$

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where W₁ is a linking group, O, NH, or S; and

treating said compound of formula IVA, IVB, IVC or IVD with a deprotecting reagent to form a compound of formula VA, VB, VC or VD:

$$R_{1} = O \longrightarrow B$$

$$R_{21} \longrightarrow Q$$

$$R_{21} \longrightarrow Q$$

$$R_{21} \longrightarrow Q$$

$$V = A$$

$$V = A$$

$$R_{1} \longrightarrow A$$

$$R_{21} \longrightarrow Q$$

$$R_{22} \longrightarrow Q$$

wherein W₅ has the formula:

$$\left\{ -W_{1}-C-X_{3}-NH_{2}^{ ext{ ; and }}
ight.$$

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(c) condensing said compound of Formula V with a compound of Formula VI:

$$O \longrightarrow N \longrightarrow NH$$

$$R_5 \longrightarrow N \longrightarrow NH$$

$$R_6$$

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VI

wherein:

R₅ is H or an amino protecting group;

R₆ is H or an amino protecting group;

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to form a compound of Formula VIIA, VIIB, VIIC, or VIID:

$$\begin{array}{c|c} W_7 & O & B \\ \hline & & \\$$

$$\begin{array}{c|c} R_1 - O & B \\ \hline & W_7 \\ q \\ \hline & R_{20} & R_{21} \\ \end{array}$$

VIID

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wherein W₇ has the Formula:

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(d) contacting said compound of Formula VIIA or VIID with a phosphitylating reagent to form a compound of Formula VIIIA or VIIID:

wherein W₇ has the Formula:

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106 (Previously Presented). A synthetic method comprising the steps of:

(a) providing a compound of formula IA, IB, IC or ID:

ΙA

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$$\begin{array}{c|c} W_1 a & O & B \\ \hline & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\$$

IC

$$R_1$$
— O — O — B
 W_1a
 q
 Q
 R_{20}
 R_{21}

ΙB

ID

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wherein:

W_{1a} is W_{1b}-H, OH, NH₂ or SH, where W_{1b} is a linking group;

 R_1 is H or a hydroxyl protecting group;

B is a nucleobase;

each R₂₁ is H, OH, F, or a group of formula Z-R₂₂-(R₂₃)_v;

Z is O, S, NH, or N-
$$R_{22}$$
- $(R_{23})_v$

 R_{22} is C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, or C_2 - C_{20} alkynyl;

R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

v is from 0 to about 10;

or R₂₁ has one of the formulas:

$$--(O)_{y_1} - (CH_2)_{y_2} - O - N - (CH_2)_{y_2} - O - E$$

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wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1 - C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

q is from zero to about 50, provided that when said compound has formula ID, q is at least 1;

M is an optionally protected internucleoside linkage;

(b) reacting said compound of formula I with a compound of formula II:

$$R_{30}$$
—NH— X_3 -C—OH

II

wherein:

R₃₀ is an amino protecting group;

 X_3 is a group of formula XI:

$$\left\{ \begin{array}{c} -(CH_2)_p \\ R \end{array} \right\}$$

XI

wherein:

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p is 1 or 2;

R₄ is a hydroxyl group, or a protected hydroxy group;

or X_3 is a group of formula XII:

$$\{\bigvee_{m}\}$$

XII

wherein m is 1 or 2;

 Z_1 is the sidechain of a naturally occurring amino acid, or a protected sidechain of a naturally occurring amino acid;

R₄ is a hydroxyl group, or a protected hydroxyl group;

p is 1 or 2; to form a compound of formula IVA, IVB, IVC, or IVD:

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$$W_{4} = \begin{bmatrix} O & B \\ R_{21} \end{bmatrix}_{q}$$

$$R_{20} = R_{21}$$

$$R_1 - O \longrightarrow O \longrightarrow B$$
 $M \longrightarrow M$
 $R_{20} \longrightarrow R_{21}$
IVD

wherein:

W₄ has the formula:

IVC

where W_1 is a linking group, O, NH, or S; and treating said compound of formula IVA, IVB, IVC or IVD with a deprotecting reagent to form a compound of formula VA, VB, VC or VD:

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$$R_{1} = 0$$

$$R_{21}$$

$$R_{21}$$

$$R_{20}$$

$$R_{3}$$

$$R_{21}$$

$$R_{4}$$

$$R_{21}$$

$$R_{1} = 0$$

$$R_{21}$$

$$R_{21}$$

$$R_{1} = 0$$

$$R_{1} = 0$$

$$R_{1} = 0$$

$$R_{21}$$

$$R_{1} = 0$$

$$R_{21}$$

$$R_{21}$$

$$R_{21}$$

$$R_{3} = 0$$

$$R_{4} = 0$$

$$R_{1} = 0$$

$$R_{1} = 0$$

$$R_{21}$$

$$R_{3} = 0$$

$$R_{4} = 0$$

$$R_{1} = 0$$

$$R_{21}$$

$$R_{3} = 0$$

$$R_{4} = 0$$

$$R_{1} = 0$$

$$R_{21} = 0$$

$$R_{21} = 0$$

$$R_{3} = 0$$

$$R_{4} = 0$$

$$R_{4} = 0$$

$$R_{5} = 0$$

$$R$$

wherein W₅ has the formula:

$$\left\{ \begin{matrix} O \\ \parallel \\ -W_1 \end{matrix} \begin{matrix} C - X_3 - NH_2 \end{matrix} \right\}$$
; and

VC

Ŕ₂₁

V D

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(c) condensing said compound of Formula V with a compound of Formula VI:

VI

wherein:

R₅ is H or an amino protecting group;

R₆ is H or an amino protecting group;

to form a compound of Formula VIIA, VIIB, VIIC, or VIID:

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$$R_{1} - O \longrightarrow B$$

$$R_{21} \longrightarrow Q$$

$$R_{21} \longrightarrow Q$$

$$R_{21} \longrightarrow Q$$

$$R_{21} \longrightarrow Q$$

$$W_{7} \longrightarrow R_{2}$$

$$VIIA$$

$$VIIB$$

$$R_{1} - O \longrightarrow B$$

$$\begin{array}{c|c} W_{7} & O & B \\ \hline & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\$$

VIIC

$$R_1$$
— O
 M
 W_7
 Q
 R_{20}
 R_{21}

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wherein W_7 has the Formula:

wherein said compound of formula VI is prepared by the steps of reacting a compound of formula IX:

with a compound of formula X:

$$H_2N$$
 C
 C
 C
 C
 C
 C

and treating the product of said reaction with a protecting group reagent to form said compound of formula VI.

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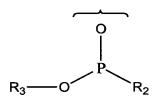
Claims 107-109 (Canceled)

110 (Previously Presented). The compound of claim 112 wherein said R_{20} is a group of formula:

$$R_3$$
— O
 R_2

wherein R_{2} is diisopropylamino and R_{3} is $\beta\mbox{-cyanoethyl}.$

111 (Previously Presented). The compound of claim 67 wherein R_{20} is a group of formula:



where R_3 is β -cyanoethyl, and R_2 is diisopropylamino.

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112 (Previously Presented). A compound having formula XVIA, XVIB, XVIC or XVID:

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$$W_{14}$$
 O
 B
 M
 R_{21}
 Q
 O
 B
 Q
 R_{20}
 R_{21}
 R_{21}

$$R_1O \xrightarrow{O} \xrightarrow{B} \\ M \xrightarrow{W_{14}} \xrightarrow{q} \\ R_{20} \xrightarrow{R_{21}}$$

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XVID

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wherein:

W₁₄ has the formula

wherein:

 X_4 is -CH(X_4) or a group of formula:

$$-(CH_2)_t$$
 R_4

X₄ is the side chain of a naturally-occurring or non-naturally-occurring amino acid, or a protected side chain of a naturally-occurring or non-naturally-occurring amino acid;

t is 1 or 2;

 X_5 is -N(X₆)C(O)-, -C(O)NH-, -NHC(O)-, -OC(O)NH-,-C(S)NH-, -SC(S)NH-, -SC(O)NH-, -OC(S)NH-, -C(O)O-, -C(O)(CH₂)_n- or a bond;

n is an integer from 1 to 50;

each X_6 and X_6 is, independently, a bond, hydrogen or a hydrocarbyl group selected from C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{20} alkynyl, C_6 - C_{14} aryl, C_6 - C_{14} aralkyl, C_3 - C_{14} cycloalkyl, C_5 - C_{14} fused cycloalkyl, C_4 - C_{14} heterocycle, C_4 - C_{14} heterocyclylalkyl, C_4 - C_{14} heteroaryl and C_4 - C_{14} heteroarylalkyl; wherein said hydrocarbyl group is substituted with at least two hydroxyl groups,

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and is optionally substituted with oxo, acyl, alkoxy, alkoxycarbonyl, alkyl, alkenyl, alkynyl, amino, amido, azido, aryl, heteroaryl, carboxylic acid, cyano, guanidino, halo, haloalkyl, haloalkoxy, hydrazino, ODMT, alkylsulfonyl, nitro, sulfide, disulfide, sulfone, sulfonate, sulfonamide, thiol, and thioalkoxy; provided that X_6 is not hydrogen and X_6 is not a bond;

 R_1 is hydrogen or a hydroxyl protecting group;

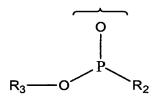
R₄ is a hydroxyl group or a protected hydroxyl group;

each $R_{5'}$ and R_{40} is, independently, hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{20} alkynyl, C_6 - C_{14} aryl or an amino-protecting group

 $R_{5"}$ is hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{20} alkynyl, C_6 - C_{14} aryl, C_6 - C_{14} aralkyl, C_3 - C_{14} cycloalkyl, formyl, aminoalkyl or hydroxymethyl;

R₆ is hydrogen or an amino protecting group;

 R_{20} is hydroxyl or a group of formula:



 R_2 is $-N(R_7)_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R₇ is straight or branched chain alkyl having from 1 to 10 carbons;

R₃ is a phosphorus protecting group;

R₂₁ is hydrogen, hydroxyl, fluoro or a group of formula Z-R₂₂-(R₂₃)_v;

Z is O, S, NH or N- R_{22} - $(R_{23})_{v}$;

 R_{22} is C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, or C_2 - C_{20} alkynyl;

R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-

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aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or R_{21} has one of the formulas:

$$-(O)_{y1}-(CH_2)_{y2}$$
 $-(CH_2)_{y3}$ $-(CH_2)_{y3}$

$$--(O)_{y1} - (CH_2)_{y2} - O - N - (CH_2)_{y2} - O - E$$

wherein:

y1 is 0 or 1; each y2 is, independently, 0 to 10; y3 is 1 to 10; E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1 - C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

B is a nucleobase;

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M is an optionally protected internucleoside linkage;

q is 0 to about 50; and

v is from zero to about 10;

provided that when said compound has formula XVID, q is at least 1.

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113 (Previously Presented). A compound having formula XVIA, XVIB, XVIC or XVID:

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wherein:

 W_{14} has the formula:

$$-X_{6}-X_{5}-X_{4}-N$$
 X_{9}
 X_{9}
 X_{1}
 X_{9}
 X_{1}
 X_{1}
 X_{1}
 X_{2}
 X_{3}
 X_{4}
 X_{5}
 X_{5}
 X_{5}
 X_{1}
 X_{1}
 X_{2}
 X_{3}
 X_{4}
 X_{5}
 X_{5}

wherein:

 X_4 is -CH(X_4) or a group of formula:

$$-(CH_2)_t$$

X₄ is the side chain of a naturally-occurring or non-naturally-occurring amino acid, or a protected side chain of a naturally-occurring or non-naturally-occurring amino acid;

t is 1 or 2;

 X_5 is -N(X_6)C(O)-, -C(O)NH-, -NHC(O)-, -OC(O)NH-, -C(S)NH-, -SC(S)NH-, -SC(O)NH-, -OC(S)NH-, -C(O)O-, -C(O)(CH₂)_n- or a bond;

n is an integer from 1 to 50;

each X_6 , X_6 and X_9 is, independently, a bond, hydrogen or a hydrocarbyl group selected from C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{20} alkynyl, C_6 - C_{14} aryl, C_6 - C_{14} aralkyl, C_3 - C_{14} cycloalkyl,

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 C_5 - C_{14} fused cycloalkyl, C_4 - C_{14} heterocycle, C_4 - C_{14} heterocyclylalkyl, C_4 - C_{14} heteroaryl and C_4 - C_{14} heteroarylalkyl; wherein said hydrocarbyl group is substituted with at least two hydroxyl groups, and is optionally substituted with oxo, acyl, alkoxy, alkoxycarbonyl, alkyl, alkenyl, alkynyl, amino, amido, azido, aryl, heteroaryl, carboxylic acid, cyano, guanidino, halo, haloalkyl, haloalkoxy, hydrazino, ODMT, alkylsulfonyl, nitro, sulfide, disulfide, sulfone, sulfonate, sulfonamide, thiol, and thioalkoxy; provided that each X_6 and X_9 is not hydrogen and X_6 is not a bond;

 R_1 is hydrogen or a hydroxyl protecting group;

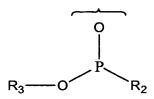
R₄ is a hydroxyl group or a protected hydroxyl group;

each $R_{5'}$ and R_{40} is, independently, hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{20} alkynyl, C_6 - C_{14} aryl or an amino-protecting group

 $R_{5"}$ is hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{20} alkynyl, C_6 - C_{14} aryl, C_6 - C_{14} aralkyl, C_3 - C_{14} cycloalkyl, formyl, aminoalkyl or hydroxymethyl;

R₆ is hydrogen or an amino protecting group;

R₂₀ is hydroxyl or a group of formula:



 R_2 is $-N(R_7)_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

 R_7 is straight or branched chain alkyl having from 1 to 10 carbons;

R₃ is a phosphorus protecting group;

 R_{21} is hydrogen, hydroxyl, fluoro or a group of formula Z- R_{22} -(R_{23}),

Z is O, S, NH or N- R_{22} - $(R_{23})_v$;

 R_{22} is C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, or C_2 - C_{20} alkynyl;

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R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or R₂₁ has one of the formulas:

$$--(O)_{y_1} - (CH_2)_{y_2} - O - N - (CH_2)_{y_2} - O - E$$

wherein:

y1 is 0 or 1; each y2 is, independently, 0 to 10; y3 is 1 to 10; E is N(R₄₁)(R₄₂) or N=C(R₄₁)(R₄₂);

each R_{41} and each R_{42} is independently H, C_1 - C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N

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or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

B is a nucleobase;

M is an optionally protected internucleoside linkage;

q is 0 to about 50; and

v is from zero to about 10;

provided that when said compound has formula XVIC, at least one R_{21} is a group other than hydrogen, and when said compound has formula XVIC or XVID, q is at least 1.

114 (Previously Presented) A compound having formula XVIA, XVIB, XVIC or XVID:

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wherein:

W₁₄ has the formula:

$$-x_6-x_5-x_4-\underset{H}{\bigvee} \overset{O}{\bigvee} \overset{R_5"}{\bigvee} \overset{CH_3}{\bigvee} \overset{O}{\bigvee} \overset{N}{\bigvee} \overset{N}{\bigvee} \overset{N}{\bigvee} \overset{R_6}{\bigvee} \overset$$

wherein:

 X_4 is -CH(X_4) or a group of formula:

$$-(CH_2)_t$$
 R_4

X_{4'} is the side chain of a naturally-occurring or non-naturally-occurring amino acid, or a protected side chain of a naturally-occurring or non-naturally-occurring amino acid;

t is 1 or 2;

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 X_5 is -N(X₆)C(O)-, -C(O)NH-, -NHC(O)-, -OC(O)NH-, -C(S)NH-, -SC(S)NH-, -SC(O)NH-, -OC(S)NH-, -C(O)O-, -C(O)(CH₂)_n- or a bond;

n is an integer from 1 to 50;

each X_6 and X_6 is, independently, a bond, hydrogen or a hydrocarbyl group selected from C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{20} alkynyl, C_6 - C_{14} aryl, C_6 - C_{14} aralkyl, C_3 - C_{14} cycloalkyl, C_5 - C_{14} fused cycloalkyl, C_4 - C_{14} heterocycle, C_4 - C_{14} heterocyclylalkyl, C_4 - C_{14} heteroaryl and C_4 - C_{14} heteroarylalkyl; wherein said hydrocarbyl group is substituted with at least two hydroxyl groups, and is optionally substituted with oxo, acyl, alkoxy, alkoxycarbonyl, alkyl, alkenyl, alkynyl, amino, amido, azido, aryl, heteroaryl, carboxylic acid, cyano, guanidino, halo, haloalkyl, haloalkoxy, hydrazino, ODMT, alkylsulfonyl, nitro, sulfide, disulfide, sulfone, sulfonate, sulfonamide, thiol, and thioalkoxy; provided that X_6 is not hydrogen and X_6 is not a bond;

 R_1 is hydrogen or a hydroxyl protecting group;

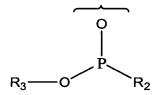
R₄ is a hydroxyl group or a protected hydroxyl group;

each R_{5} and R_{40} is, independently, hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{20} alkynyl, C_6 - C_{14} aryl or an amino-protecting group

 $R_{5"}$ is hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{20} alkynyl, C_6 - C_{14} aryl, C_6 - C_{14} aralkyl, C_3 - C_{14} cycloalkyl, formyl, aminoalkyl or hydroxymethyl;

R₆ is hydrogen or an amino protecting group;

R₂₀ is hydroxyl or a group of formula:



 R_2 is $-N(R_7)_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R₂ is straight or branched chain alkyl having from 1 to 10 carbons;

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R₃ is a phosphorus protecting group;

 R_{21} is hydrogen, hydroxyl, fluoro or a group of formula $Z-R_{22}-(R_{23})_v$;

Z is O, S, NH or N- R_{22} - $(R_{23})_v$;

 R_{22} is C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, or C_2 - C_{20} alkynyl;

R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or R_{21} has one of the formulas:

$$-(CH_2)_{y_2}$$
 $O - E$

$$--(O)_{y1} - (CH_2)_{y2} - O - N - (CH_2)_{y2} - O - E$$

wherein:

y1 is 0 or 1; each y2 is, independently, 0 to 10; y3 is 1 to 10; E is N(R₄₁)(R₄₂) or N=C(R₄₁)(R₄₂);

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each R_{41} and each R_{42} is independently H, C_1 - C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

B is a nucleobase;

M is an optionally protected internucleoside linkage;

q is 0 to about 50; and

v is from zero to about 10;

provided that when said compound has formula XVID, q is at least 1.

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115 (Previously Presented) A compound having the formula XIIIA, XIIIB, XIIIC or XIIID:

XIIID

R₂₁

 $\dot{\mathbf{W}}_{13}$

XIIIB

wherein:

W₁₃ has the formula:

$$\{-W_1-C-X_3-NH \}$$

 \dot{R}_{20}

XIIIC

Ŕ₂₁

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R₁ is H or a hydroxyl protecting group;

B is a nucleobase;

each R₂₁ is H, OH, F, or a group of formula Z-R₂₂-(R₂₃)_v;

Z is O, S, NH or N- R_{22} - $(R_{23})_{v}$;

 R_{22} is C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, or C_2 - C_{20} alkynyl;

R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or R_{21} has one of the formulas:

$$- \left[(O)_{y1} - (CH_2)_{y2} \right]_{y_3} O - E$$

$$- (O)_{y1} - (CH_2)_{y2} - O - N - (CH_2)_{y2} - O - E$$

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wherein:

y1 is 0 or 1; y2 is 0 to 10; y3 is 1 to 10; E is N(R₄₁)(R₄₂) or N=C(R₄₁)(R₄₂);

each R_{41} and each R_{42} is independently H, C_1 - C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

v is from 0 to about 10;

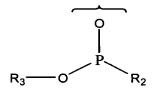
q is 0 to about 50; and

v is from zero to about 10;

M is an optionally protected internucleoside linkage;

 W_1 is a linking group, O, NH or S;

R₂₀ is hydroxyl or a group of Formula;



 R_2 is $-N(R_7)_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

 R_7 is straight or branched chain alkyl having from 1 to 10 carbons;

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R₃ is a phosphorus protecting group;

R₅ is H or an amino protecting group;

R₆ is H or an amino protecting group;

X₃ has the formula XII:

$$\{\bigcup_{m}\}$$

XII

wherein m is 1 or 2; and

 R_4 is a hydroxyl group, or a protected hydroxyl group; provided that when said compound has formula XIIIC, at least one R_{21} is a group other than hydrogen, and when said compound has formula XIIIC or XIIID, q is at least 1.

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116 (Previously Presented) A compound having the formula XVIA, XVIB, XVIC or XVID:

$$W_{16} = \begin{bmatrix} O & B \\ & &$$

XVIC

XVIB

PATENT

XVID

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wherein:

W₁₆ has the formula:

R₁ is H or a hydroxyl protecting group;

B is a nucleobase;

each R₂₁ is H, OH, F, or a group of formula Z-R₂₂-(R₂₃)_v;

Z is O, S, NH or N- R_{22} - $(R_{23})_v$;

 $R_{22} \text{ is } C_1\text{-}C_{20} \text{ alkyl, } C_2\text{-}C_{20} \text{ alkenyl, } C_2\text{-}C_{20} \text{ alkynyl, } C_1\text{-}C_{20} \text{ akoxy, } C_2\text{-}C_{20} \\$ alkenyloxy, or $C_2\text{-}C_{20}$ alkynyloxy;

R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or R_{21} has one of the formulas:

$$-[(O)_{y1}-(CH_2)_{y2}]_{y3}O-E$$

$$----(O)_{y_1} - \underbrace{\begin{pmatrix} CH_2 \end{pmatrix}_{y_2} - O - N - \begin{pmatrix} R_{41} \\ V_{1} \\ V_{2} \end{pmatrix}}_{y_3} + \underbrace{\begin{pmatrix} CH_2 \end{pmatrix}_{y_2} - O - E}_{y_3}$$

wherein:

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y1 is 0 or 1; y2 is 0 to 10; y3 is 1 to 10;

E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1 - C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

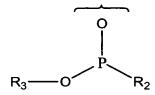
v is from 0 to about 10;

q is 0 to about 50;

M is an optionally protected internucleoside linkage;

W₁ is a linking group;

 R_{20} is hydroxyl or a group of Formula:



 R_2 is $-N(R_7)_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R₇ is straight or branched chain alkyl having from 1 to 10 carbons;

R₃ is a phosphorus protecting group;

 X_3 has the formula XII:

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XII

wherein m is 1 or 2;

 R_4 is a hydroxyl group, or a protected hydroxyl group; and provided that when said compound has formula XVID, q is at least 1.

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117 (Previously Presented) A compound having the formula XVIIA, XVIIB, XVIIC or XVIID:

 R_{20} R_{21}

XVIIC

$$R_1$$
— O
 M
 W_{17}
 Q
 R_{20}
 R_{21}

 $\dot{W}_{17} \dot{R}_{21}$

XVIID

XVIIB

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wherein:

W₁₇ has the formula:

$$\{-w_1 - \overset{O}{C} - x_3 - NH$$

$$\downarrow \\ R_5$$

R₁ is H or a hydroxyl protecting group;

B is a nucleobase;

each R₂₁ is H, OH, F, or a group of formula Z-R₂₂-(R₂₃)_v;

Z is O, S, NH or N- R_{22} - $(R_{23})_v$;

 R_{22} is C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, or C_2 - C_{20} alkynyl;

R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or R_{21} has one of the formulas:

$$-(O)_{y1}-(CH_2)_{y2}$$
 $O-E$

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wherein:

y1 is 0 or 1; y2 is 0 to 10; y3 is 1 to 10;

E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1 - C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

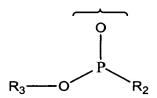
v is from 0 to about 10;

q is 0 to about 50;

M is an optionally protected internucleoside linkage;

W₁ is a linking group, O, NH or S;

R₂₀ is hydroxyl or a group of Formula:



 R_2 is $-N(R_7)_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R₇ is straight or branched chain alkyl having from 1 to 10 carbons;

R₃ is a phosphorus protecting group;

 X_3 has the formula XII:

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XII

wherein m is 1 or 2;

R₄ is a hydroxyl group, or a protected hydroxyl group; and

R₅ is H or an amino protecting group;

provided that when said compound has formula XVIID, q is at least 1.